# Original Research Communications—general

# Relationship of catecholamine excretion to body size, obesity, and nutrient intake in middle-aged and elderly men<sup>1-3</sup>

James B Young, Rebecca J Troisi, Scott T Weiss, Donna R Parker, David Sparrow, and Lewis Landsberg

**ABSTRACT** Catecholamine release from sympathetic nerves and the adrenal medulla is influenced by diet under controlled research conditions. To test whether diet affects catecholamine excretion in free-living men, the urinary content of dopamine (DA), epinephrine (Epi), or norepinephrine (NE) was measured in 24-h collections provided by 572 participants of the Normative Aging Study of the Veterans Administration. Average daily intakes of energy and macronutrients were assessed by means of a semiquantitative food frequency questionnaire and sodium intake by quantitation of sodium excretion. Catecholamine excretion was also examined in relation to anthropometric variables. Because DA and Epi excretion were inversely related to age, all subsequent analyses included adjustments for age. Although DA and NE were positively related to measures of body size and fatness, Epi was negatively related to body fatness. Excretion rates of all three catecholamines were directly related to total energy intake and inversely related to energyadjusted CHO consumption. Am J Clin Nutr 1992;56: 827-34.

**KEY WORDS** Age, fat, energy intake, norepinephrine, carbohydrate, obesity, dopamine, protein, epinephrine, sodium

# Introduction

Accumulating evidence suggests that the catecholamines dopamine (DA), norepinephrine (NE), and epinephrine (Epi), excreted as free amines in urine, originate primarily from different components of a peripheral chromaffin system (or systems). Epi derives principally from the adrenal medulla and NE from peripheral sympathetic nerves, although under stressful conditions the adrenal medullary release of NE may also be quantitatively important (1). DA, in contrast, predominantly reflects renal decarboxylation of circulating 3,4-dihydroxyphenylalanine (DOPA) in proximal tubular cells (2-4). Dietary intake differentially affects the activity of these chromaffin systems, differences that can be observed in the urinary excretion of DA, NE, and Epi in metabolic studies in animals (5-8) or in human subjects (1, 6, 9, 10). Whether any of these dietary factors are important determinants of urinary catecholamine excretion in humans outside of a clinical research protocol is, however, not

The present study is part of an investigation of potential health consequences, especially in relation to cardiovascular disease,

of individual differences in sympathoadrenal activity as reflected in urinary catecholamine excretion. Because dietary and constitutional variables were measured in addition to catecholamine excretion, the study provided an opportunity to test whether dietary composition is an important determinant of sympathoadrenal activity in a free-living population, as it is in animals and human subjects under more controlled circumstances. This report examined the impact of dietary intake, age, and anthropometric variables on catecholamine excretion in a sample of 572 participants in the Normative Aging Study of the Veterans Administration (11). Urinary excretion of NE, but not of Epi, was reported previously to be related positively to obesity [body mass index (BMI) and abdomen-hip ratio], total energy intake, and insulin-glucose status (12, 13).

# Methods

Study subjects

The Normative Aging Study is an ongoing longitudinal, multidisciplinary study established by the Veterans Administration in 1963. Details of the study protocol were presented elsewhere (11). Male volunteers were initially selected on the basis of clinical, laboratory, radiological, and electrocardiographic criteria to provide a healthy population at outset. A history or the presence of coronary heart disease, diabetes mellitus, cancer, peptic ulcer, gout, recurrent asthma, or bronchitis were criteria for exclusion from the study. Subjects were also excluded if their systolic blood pressure was > 140 mm Hg or if their diastolic blood pressure was > 90 mm Hg. Body composition and circulating lipid concentrations were not screening criteria. Although neither

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<sup>&</sup>lt;sup>1</sup> From the Charles A Dana Research Institute, Thorndike Laboratory, and Channing Laboratory, Department of Medicine, Harvard Medical School, Beth Israel Hospital, and Brigham and Women's Hospital, Boston.

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<sup>&</sup>lt;sup>3</sup> Address reprint requests to JB Young, Northwestern University Medical School, Searle Bldg 3-489, 320 East Superior Street, Chicago, IL 60611.

racial nor ethnic origin was a selection criterion, study participants are almost all Caucasian men. Subjects were aged 62.2  $\pm$  7.9 y ( $\bar{x} \pm$  SD), range 43-85 y.

# Subject examinations

Subjects report for examinations every 3-5 y. Each examination includes a physical examination and blood and urine tests. Subjects undergo an oral glucose-tolerance test (100 g) after overnight abstinence from food or tobacco. In addition, a series of anthropometric measurements are made on each participant with the subject dressed only in undershorts and socks, standing erect with feet together. Weight is measured on a balance-beam scale to the nearest 0.5 lb and converted to kilograms. Height is measured against a wall chart to the nearest 0.1 in and converted to centimeters. BMI is calculated as weight (in kg) divided by height<sup>2</sup> (in m). Abdomen circumference is measured to the nearest 0.1 cm at the level of the umbilicus perpendicular to the axis of the body. Hip circumference is measured to the nearest 0.1 cm at the greatest protrusion of the buttocks. Abdomen-hip ratio refers to the ratio of these two measures of body circumference. The participants are also categorized as never, current, or former smokers on the basis of personal interview. To be considered a former smoker the subject must have refrained from smoking for  $\geq 1$  y.

### Dietary questionnaire

Dietary data for this study were obtained from a semiquantitative food frequency questionnaire (FFQ) (14, 15). Subjects received the FFQ in the mail and filled it out before their visit to the study center. Questionnaires were coded by a research assistant and then checked by two other observers (RJT, DRP). A nutritionist who was involved in the development of the FFQ was consulted when coding was found to be inconsistent among the three coders. The FFQ listed food items with serving sizes and asked about frequency of intake. Nutrient scores were computed by multiplying the frequency of intake by the nutrient content of the food item. Average daily intake of total energy and of individual macronutrients (protein, carbohydrate, and fat) was estimated. Variables representing energy-adjusted macronutrient intakes were computed as described by Willett (16). Residuals from the regression of absolute macronutrient intake on total energy were added to the value for macronutrient intake on the regression line at the mean total energy intake for the study sample. Caffeine intake was estimated from responses to questions concerning coffee, tea, chocolate, and cola-beverage consumption.

The FFQ also provided information on physical activity. Based on Paffenbarger et al's scale (17), responses to questions asking number of flights of stairs climbed per day, walking pace, and frequency of various physical activities were used to derive a continuous physical-activity variable that assessed total energy expenditure in MJ/wk.

All procedures followed were in accord with the ethical standards of the Human Studies Subcommittee of the Research and Development Committee, Department of Veteran Affairs Outpatient Clinic, Boston.

# Biochemical analysis

Twenty-four-hour urine samples were collected at home by participants and brought in at the time of their routine examination. In addition, a questionnaire eliciting information on urine collection times, missed collections, spillage, and medication use was completed by the subject. Urine samples were collected under oil in polyethylene containers in the presence of 15 mL 6 mol HCl/L and 0.5 g sodium metabisulfite and were analyzed for catecholamines by liquid chromatography with electrochemical detection according to the method of Smedes et al (18) as modified by Macdonald and Lake (19). The intraassay coefficients of variation for urine samples (corrected for recovery) were 4-6% for each catecholamine. The interassay coefficients of variation were 6-7%. Urinary sodium was measured by flame photometry; the results were not corrected for the 5 mmol added as sodium metabisulfite.

# Exclusions

Data were collected from examinations conducted between February 1987 and June 1989. Of 889 subjects examined during this time, 717 (81%) provided a 24-h urine sample. A total of 43 urine samples were excluded: 8 samples because volumes were < 500 mL, 9 samples because the collection time was < 15 h, 5 samples because subjects reported an incomplete collection, 5 samples because questionnaires were missing, and 16 samples because subjects were taking L-DOPA, methyldopa, or thorazine on the day of their urine collection. Five additional subjects were excluded from the analysis because their total daily energy intake from the FFQ was not within the range set a priori (2.51-19.25 MJ/d) and was assumed to reflect either under- or overreporting. Sixty-seven observations had to be excluded because of missing values for one or more of the study variables. Finally, 30 subjects taking insulin were excluded. After elimination of these 145 cases, data from 572 subjects were available for analysis.

# Statistical analyses

Table 1 presents the descriptive statistics for the study sample. Comparisons between the study sample and exclusions in age, body habitus, urinary catecholamines, dietary intake, and physical activity were done with t tests. Only height was significantly different between the included and excluded cases; subjects excluded from the study sample were shorter on average (1.74)

TABLE 1
Characteristics of study sample\*

Variables	Value
Age (y)	$62.2 \pm 7.9$
Weight (kg)	$82.0 \pm 12.5$
Height (m)	$1.76 \pm 0.06$
BMI†	$26.5 \pm 3.5$
Abdomen circumference (cm)	$100.4 \pm 9.3$
Hip circumference (cm)	$102.6 \pm 7.1$
Abdomen-hip ratio	$0.978 \pm 0.047$
Total energy (MJ/d)	$8.38 \pm 2.67$
Physical activity (MJ/wk)	$7.30 \pm 7.32$
Urinary catecholamines (µg/24 h)	
Dopamine	$334.4 \pm 121.2$
Epinephrine	$6.8 \pm 3.8$
Norepinephrine	48.0 ± 20.1

<sup>\*</sup>  $\bar{x} \pm SD$ .

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<sup>†</sup> In kg/m<sup>2</sup>.

TABLE 2
Pearson product-moment correlations for urinary catecholamines\*

Variables	Dopamine	ln (epinephrine)	ln (norepinephrine)
Age	-0.226†	-0.184†	0.073
Physical activity (as ln)	-0.083‡	0.010	0.074
Urinary-excretion variables			
Epinephrine (as In)	0.338†	_	
Norepinephrine (as ln)	0.521†	0.408†	_
Sodium	0.146§	0.104‡	0.085

<sup>\*</sup> n = 572, except for sodium (n = 472). In, natural logarithm.

 $\pm$  0.08 m for exclusions vs 1.76  $\pm$  0.06 for study sample;  $\bar{x}$   $\pm$  SD). BMI was also slightly, though not significantly, higher in those excluded (P = 0.07).

Pearson product-moment correlations were calculated between the individual catecholamines and age, body-habitus variables, dictary variables, urinary sodium, and physical activity. Analysis of covariance was used to compare DA values by tertile of anthropometric and dietary variables after adjustment for age. [Similar analyses for NE and Epi were presented previously (13)]. Multiple linear-regression analysis was used to assess the independent relationships of BMI, height, abdomen-hip ratio, dietary intake, and urinary sodium to catecholamine excretion while age was controlled for.

Normal probability plots were examined to determine whether any of the variables that would be used in the linear regressions needed skewness-reducing transformations to improve the linearity assumption for these variables. As a result, urinary NE, urinary Epi, and physical-activity data were transformed into natural logarithms before analysis. Residuals were generated from the final multiple linear-regression models to determine goodness of fit. All statistical analyses were performed by using Statistical Analysis System AOS/VS version 5.18 (20). P values < 0.05 were considered statistically significant.

# Results

Pearson product-moment correlations for DA, Epi, and NE and individual study variables are presented in Tables 2, 3, and

6. [Correlations between ln(Epi) or ln(NE) and age, BMI, abdomen circumference, abdomen-hip ratio, total energy, and physical activity were presented previously (13) and are included here for comparison with DA; ln is natural logarithm]. As indicated in Table 2, all three catecholamines were inversely related to age although only with DA and Epi was this correlation statistically significant. As noted previously (21), urinary DA, Epi, and NE were all highly correlated with one another. DA and Epi were also positively related to urinary sodium content.

In addition, DA, but neither Epi nor NE, was weakly and inversely related to the natural logarithm of physical activity. This relationship between DA and physical activity, however, was not evident when the effect of age was also included in the analysis. In contrast to a previous report that urinary Epi was positively related to cigarette smoking (22), in this study urinary excretion of none of the catecholamines, including Epi, was related to smoking status (current, former, never) when age was included in the model (P = 0.7011, 0.1565, and 0.7854, respectively).

Correlations among age, urinary catecholamines, and anthropometric variables are presented in Table 3 and comparisons of DA excretion among tertiles of anthropometric variables are shown in Table 4. Although anthropometric variables were generally inversely related to age and less strongly to urinary Epi, they are positively related to both DA and NE. Within the set of anthropometric variables used, height was not correlated with either BMI or abdomen-hip ratio, although BMI was highly correlated with weight, abdominal circumference, and abdomenhip ratio. Consequently, the multiple-regression models examining the influence of anthropometric variables and urinary catecholamine excretion used height and either BMI or abdomen-hip ratio. (In these models height was included as a measure of body size because BMI is generally regarded as a size-independent measure of body fatness). The results of these analyses are presented in Table 5.

DA excretion was positively related to BMI and height and negatively related to age in a model in which all three variables accounted for 11% of the total variation in urinary DA. DA was also significantly related to abdomen-hip ratio when age and height were included (P = 0.0058), but not if BMI was also included. Similar regression models for Epi and NE demonstrated that only two of the three independent variables were significantly related to amine excretion and, consequently, accounted for a smaller fraction of the total variance (4% and 7%,

TABLE 3
Correlation matrix for anthropometric variables with age and urinary catecholamine excretion

	Weight	Height	вмі	Abdomen circumference	Abdomen-hip ratio
Age	-0.286*	-0.270*	-0.180*	-0.142*	-0.017
Dopamine	0.305*	0.127†	0.275*	0.253*	0.115†
In (epinephrine)	-0.041	0.007	-0.051	-0.109†	-0.090‡
In (norepinephrine)	0.265*	0.091‡	0.254*	0.278*	0.157*
Weight		0.473*	0.877*	0.872*	0.397*
Height			-0.004	0.249*	-0.008
BMI				0,856*	0.454*
Abdomen circumference					0.684*

<sup>\*</sup> P < 0.001.

<sup>†</sup> P < 0.001.

<sup>+</sup> P < 0.05

 $<sup>\</sup>delta P < 0.01$ 

<sup>+</sup> P < 0.01.

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TABLE 4
Rates of dopamine excretion (age-adjusted) within tertiles of anthropometric variables\*

					P values	
	I	II	m	I vs II	I vs III	II vs III
	μg/24 h	μg/24 h	μg/24 h			
Weight (kg)	$319.97 \pm 8.58$	320.42 ± 8.52	362.55 ± 8.56	0.9708	0.0006	0.0005
	(47.2-75.5)	(75.5-85.5)	(85.5-149.8)			210002
Height (cm)	$324.02 \pm 8.79$	334.09 ± 8.56	$344.84 \pm 8.60$	0.4143	0.0957	0.3740
	(157.4-172.7)	(172.7-178.5)	(178.5-195.6)			0.57.10
Body mass index†	$324.73 \pm 8.54$	$318.98 \pm 8.47$	$359.46 \pm 8.50$	0.6333	0.0043	0.0008
	(15.26-25.03)	(25.03-27.61)	(27.61-47.13)			
Abdominal circumference (cm)	$314.54 \pm 8.49$	$328.83 \pm 8.48$	$359.82 \pm 8.48$	0.2342	0.0002	0.0100
	(70.5-96.5)	(96.5-103.7)	(103.7-148.7)			272254
Abdomen-hip ratio	$320.79 \pm 8.50$	$323.10 \pm 8.48$	$359.26 \pm 8.47$	0.8473	0.0014	0.0027
	(0.82-0.96)	(0.96-1.00)	(1.00-1.12)	-		

<sup>\*</sup>  $\bar{x} \pm SE$  (range).

respectively). Epi was negatively related to both age and BMI whereas NE was positively related to BMI and height. For both Epi and NE, similar findings were obtained when abdomen-hip ratio replaced BMI in the model. Thus, both DA and NE were positively related to body size (height) and body fatness (BMI or abdomen-hip ratio) whereas Epi was negatively related to fatness but not to size.

A similar approach was taken to examine the relationships among urinary catecholamines and dietary variables, including urinary sodium as an index of sodium intake (Tables 6 and 7). Amine excretion was positively related to intake of energy and, less so, to intake of fat (adjusted for total energy) and negatively related to carbohydrate (CHO) intake (adjusted for total energy). Although a positive association between Epi excretion and coffee consumption was reported previously (22), in this study caffeine intake was not correlated with urinary excretion of any of the catecholamines. By definition, nutrient intake after adjustment for energy intake did not correlate with total energy, although intakes of fat, CHO, and protein were highly correlated with one another. Consequently, the multiple-regression models examining the influence of dietary variables and urinary catecholamine excretion used only total energy and either CHO or fat intake, in addition to age. Furthermore, because sodiumexcretion data were available for only 472 subjects, dietary models were run both with and without this variable. The results of these analyses are presented in Table 8.

DA excretion was positively related to total energy and negatively related to CHO intake and age in a model in which all three variables accounted for 9% of the total variation in urinary DA. These three variables remained significant predictors of urinary DA in a second model after addition of urinary sodium, which was also positively related to DA excretion, though of borderline statistical significance. In a similar analysis that used fat instead of CHO, urinary DA was positively associated with adjusted fat intake (P = 0.0005), but when both fat and CHO were included, only the negative association of adjusted CHO with DA was statistically significant (P = 0.006). Regression models for Epi and NE likewise demonstrated significant associations between energy and CHO intakes and amine excre-

tion. Both were positively related to total energy and negatively related to adjusted CHO, though Epi only marginally. Inclusion of urinary sodium in the model eliminated the associations between dietary variables and Epi, but not NE. Excretion of neither Epi nor NE was related to adjusted fat intake in models, which also included age and total energy (results not shown). For all three catecholamines the influence of dietary factors on amine excretion was independent of that of anthropometric variables because all associations, except those with height, remained statistically significant when the models in Tables 5 and 8 were combined. Thus, excretion rates for all three catecholamines are positively related to energy intake and negatively related to CHO intake after adjustment for total energy. These dietary effects are largely independent of those effects due to anthropometry.

TABLE 5
Relationship of urinary catecholamines to age, BMI, and height

	β	SE (β)	P
Urinary dopamine			
Age	-2.4382	0.6392	0.0002
BMI	8.3773	1.3649	0.0001
Height	1.5956	0.7733	0.0395
		Adji	usted
		$R^2 =$	0.1100
ln (urinary epinephrine			
Age	-0.0123	0.0025	0.0001
BMI	-0.0114	0.0053	0.0331
Height	-0.0036	0.0030	0.2374
		Adjusted	
		$R^2 = 0$	0.0383
In (urinary norepinephrine)			
Age	-0.0001	0.0020	0.9452
BMI	0.0271	0.0044	0.0001
Height	0.0054	0.0025	0.0299
		Adi	usted
			0.0684

<sup>†</sup> In kg/m<sup>2</sup>.

TABLE 6
Correlation matrix for dietary-intake variables with age and urinary catecholamine excretion

	Total energy	Fat*	Carbohydrate*	Protein*	Caffeine
Age	0.019	0.079	0.144†	0.068	-0.185†
Dopamine	0.129‡	0.157+	-0.199†	0.025	0.046
In (epinephrine)	0.091§	0.015	-0.102§	0.020	0.011
In (norepinephrine)	0.108‡	0.045	-0.161†	0.088§	0.004
Urinary sodium $(n = 472)$	0.126‡	0.105§	-0.064	0.060	0.087
Total energy	<u> </u>	0.000	0.000	0.000	0.1048
Fat (adjusted for total energy)			0.564 <b>†</b>	0.200 †	0.104
Carbohydrate (adjusted for total energy)			<u> </u>	-0.353†	-0.055
Protein (adjusted for total energy)				<del></del> `	-0.077

<sup>\*</sup> Adjusted for total energy.

# Discussion

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This report demonstrates that anthropometric and dietary factors as well as age account for a substantial fraction (>14%) of the interindividual variation in DA excretion in a cohort of middle-aged and elderly Caucasian men. Variance attributable to these same factors was less for Epi and NE, 5% and 9%, respectively. Because these urine samples were obtained while the men followed their normal daily routines, there was less control of dietary, activity, and collection variables than there is within a clinical research protocol. On the other hand, one advantage of the current approach is that the associations identified in these data are potentially more reflective of the relative importance of individual study variables under real-life conditions. Moreover, the findings from this study, in general, agree with results obtained from clinical investigations in this and other laboratories, which lend support to the observations described herein.

The goal of this study was to describe the linear relationships between urinary excretion of the three catecholamines and various anthropometric and dietary factors, alone and in combination. The variables most strongly correlated with excretion of any one catecholamine were excretion rates for the other two catecholamines (Table 2), a phenomenon that was noted previously (21). The strength of these associations presumably reflects the impact of collection factors, the similarities in renal handling of biogenic amines (23), and the coordinate regulation of those portions of the peripheral sympathoadrenal system from which the individual amines originated, as well as other factors. The regression models presented in Tables 5 and 8, however, did not attempt to include catecholamine excretion as a predictive, rather than as a predicted, variable because the strong associations among catecholamine excretion rates would obscure any effects of the other variables, which together accounted for ≤ 14% of the variance in excretion of any catecholamine. Rather, given the limitations inherent in a cross-sectional study such as this, comparisons among the three catecholamines in their relationships to the factors of interest were restricted to the qualitative effects summarized in Table 9.

In this population of middle-aged and elderly men, excretion rates for DA and Epi, but not NE, were strongly and inversely related to the age of the subject. In previous reports the effect of age on NE and Epi excretion in healthy men has been variable

TABLE 7
Rates of dopamine excretion (age-adjusted) within tertiles of dietary variables\*

					P values	
	I	II	III	I vs II	I vs III	II vs III
	μg/24 h	μg/24 h	μg/2 <b>4</b> h			
Total energy intake (MJ)	$320.97 \pm 8.55$ $(2.77-7.12)$	$330.64 \pm 8.53$ (7.12-9.12)	$351.55 \pm 8.52$ (9.12-18.63)	0.4243	0.0115	0.0836
Protein intake (as % of total energy)	$343.27 \pm 8.58$ (5.8–15.0)	$330.72 \pm 8.56$ $(15.0-17.2)$	$329.28 \pm 8.55$ (17.2-29.1)	0.3012	0.2492	0.9055
Total fat intake (as % of total energy)	$322.82 \pm 8.51$ (11.2-28.1)	$322.38 \pm 8.48$ (28.1-33.0)	$357.97 \pm 8.50$ (33.0-48.7)	0.9702	0.0037	0.0032
Carbohydrate intake (as % of total energy)	$359.26 \pm 8.47$ (29.6-46.4)	$336.21 \pm 8.44$ (46.4-53.0)	$307.88 \pm 8.49$ (53.0-85.7)	0.0541	0.0001	0.0189
Urinary sodium (mmol/24 h) (n = 472)	$310.52 \pm 9.25$ (33.5-127)	$331.68 \pm 9.21$ $(127-179)$	$336.96 \pm 9.34$ $(179-375)$	0.1044	0.0463	0.6889

<sup>\*</sup>  $\vec{x} \pm SE$  (range).

 $<sup>\</sup>dagger P < 0.001$ .

P < 0.01.

 $<sup>\</sup>S P < 0.05$ .

TABLE 8
Relationship of urinary catecholamines to age, total energy, and adjusted carbohydrate, with and without urinary sodium

	Without urinary sodium $(n = 572)$			With u	rinary sodium (n =	472)
	β	SE (β)	P	β	SE (β)	P
Urinary DA						
Agc	-3.1313	0.6170	1000.0	-2.7963	0.6646	0.0001
Total energy	0.0251	0.0076	0.0009	0.0197	0.0082	0.0001
Adjusted total carbohydrate	0.4796	0.1138	0.0001	-0,4704	0.1267	0.0002
Urinary sodium	_			0.1678	0.0875	0.0557
		Adjusted R	$^2 = 0.0924$		Adjusted R	
ln (urinary epinephrine)						
Age	-0.0100	0.0024	0.0001	-0.0099	0.0026	0.0002
Total energy	0.00007	0.00003	0.0208	0.00003	0.00003	0.3783
Adjusted total carbohydrate	-0.0008	0.0004	0.0638	-0.0007	0.0005	0.1830
Urinary sodium		****		0.0005	0.0003	0.1766
		Adjusted R	$^{2} = 0.0435$		Adjusted R	
In (urinary norepinephrine)		•				
Age	-0.0026	0.0020	0.1996	-0.0037	0.0022	0.0974
Total energy	0.00006	0.00002	0.0082	0.00006	0.00003	0.0174
Adjusted total carbohydrate	-0.0014	0.0004	0.0002	-0.0012	0.0004	0.0054
Urinary sodium		_		0.0003	0.0003	0.2986
		Adjusted R	$^2 = 0.0353$		Adjusted R	

(24-26), but one population study observed generally negative correlations between Epi and age and, among Caucasian men, no relation between NE and age (27). Earlier data of Kärki (28), however, suggest that in men the relationship between Epi and age may be a biphasic one with excretion rates rising into the fifth decade and falling thereafter. If correct, the age range studied would determine whether an effect of age was observed and would explain why the findings from the current study (age range 43-85 y) were so strongly negative. The impact of age on DA excretion has been less well studied. Several reports suggested

TABLE 9
Summary of impact of independent variables on urinary catecholamine excretion

	Catecholamine excretion					
	Dopamine	In (epinephrine)	In (norepinephrine)			
Age	*		0†			
BMI	+‡	_	+			
Height	+	0	+			
Abdomen-hip ratio	+	_	+			
Total energy	+	(+) <b>§</b>	+			
Carbohydrate		· / •				
(adjusted)		(-)	-			
Fat (adjusted)	(+)	o o	0			
Protein (adjusted)	o	0	(+)			
Urinary sodium	(+)	(+)	o´			

<sup>\*</sup> A statistically significant negative association.

no effect (25, 26, 29), although one study of men and women aged ≥ 80 y noted slightly increased urinary DA in the older age group (30). Support for the current finding of an age-related decline in DA excretion comes from the recent observations of age-related reductions in DA output during daytime hours in women (31) and in men after a single protein meal (32). Thus, the current observation of inverse relations between age and urinary excretion of Epi and DA are consistent with data from other studies, including ones performed under clinical research conditions. Although the present findings provide no insight into potential mechanisms for the age-related reductions in Epi and DA excretion, they do emphasize the potential confounding effect of subject age in studies examining the impact of other variables on urinary catecholamine excretion.

Catecholamine excretion in humans, as well as in animals, is clearly influenced by body size, though the precise relation between them has not been delineated. As in our previous report (12), urinary NE excretion correlated positively with indices of body fatness and, in some regression models, with an additional index of body size (height). The present report extends this analysis by showing that, after adjustment for age, DA excretion is also positively related to both body size and fatness. In contrast to NE and DA, however, urinary Epi is an inverse function of fatness as related to either BMI or abdomen-hip ratio. The results of the current study generally agree with those of previous studies correlating urinary NE and Epi excretion with body weight, BMI. or intraabdominal fat by computed tomography (27, 33). The relations among these anthropometric variables and urinary NE and Epi excretion are also consistent with studies on the side of the debate concerning sympathoadrenal function in human obesity, which support enhanced sympathetic nervous system activity and reduced adrenal medullary secretion in this condition (34-37). On the other hand, the positive association between DA excretion and body fatness, though statistically clear, is of uncertain physiological importance.

<sup>†</sup> No statistically significant association between excretion of a catecholamine and a particular variable.

<sup>‡</sup> A statistically significant positive association.

<sup>§</sup> Symbols in parentheses indicate that the relationship is not consistently observed in the presence of other study variables.

The effect of dietary intake on catecholamines in peripheral tissues has been a major focus of this laboratory for the past 15 y. Results from these investigations and those of other laboratories suggest that individual nutrients exert differential effects on peripheral catecholamines (8). In contrast to previous prospective studies, however, in which the impact of prescribed changes in diet on indices of catecholamine release were examined, the current investigation analyzed retrospectively the relationships between diet and urinary catecholamines by using the recently developed FFQ of Willett and et al (15). Although this provides a measure of an individual's average nutrient intake over the past year, it is not necessarily indicative of dietary intake at the particular time when urine was collected for catecholamine analysis. Despite this recognized potential limitation in study design, excretion of all three catecholamines related positively to total energy intake and negatively to CHO intake (adjusted for total energy) in most analyses. On the other hand, only DA excretion was related (positively) to fat intake (adjusted for total energy). Because this association was not observed when CHO intake was also included in regression models, the relationships of DA excretion with fat and with CHO intake are not statistically distinguishable.

The effects of nutrient intake on catecholamine excretion noted in this study are more similar for the various nutrients than are findings previously reported from this laboratory (8). Several factors are likely to contribute to the relative homogeneity in response. 1) The investigative approach used here lacks sensitivity because nutrient data, even in combination with age, accounted for only 3-9% of the total variance in catecholamine excretion (Table 8). 2) Although in this analysis the effects of individual nutrients were mathematically separable from those for total energy, those among nutrient groups were not. For example, the positive association between DA and dietary fat may be equivalent to the negative one between DA and CHO. 3) In freely living subjects total energy intake (and all factors related directly to overall food consumption, such as mineral intake) may be a more important determinant of catecholamine excretion than is intake of any individual nutrient. 4) Diet-induced changes in renal function, whether related to catecholamine effects or not, may affect the excretion of all three catecholamines similarly. Nonetheless, the approach used in the present study represents an initial attempt to address in the field questions that heretofore have been asked only under more carefully controlled circumstances.

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# References

- Young JB, Rosa RM, Landsberg L. Dissociation of sympathetic nervous system and adrenal medullary responses. Am J Physiol 1984;247:E35-40.
- Oates NS, Ball SG, Perkins CM, Lee MR. Plasma and urine dopamine in man given sodium chloride in the diet. Clin Sci 1979;56: 261-4.
- 3. Lee MR. Dopamine and the kidney. Clin Sci 1982;62:439-48.
- Zimlichman R, Levinson PD, Kelly G, Stull R, Keiser HR, Goldstein DS. Derivation of urinary dopamine from plasma dopa. Clin Sci 1988:75:515-20.

- Landsberg L, Young JB. Fasting, feeding and regulation of the sympathetic nervous system. N Engl J Med 1978;298:1295-301.
- Ball SG, Oats NS, Lee MR. Urinary dopamine in man and rat: effects of inorganic salts on dopamine excretion. Clin Sci Mol Med 1978;55:167-73.
- Young JB, Kaufman LN, Saville ME, Landsberg L. Increased sympathetic nervous system activity in rats fed a low-protein diet. Am J Physiol 1985;248:R627-37.
- Kaufman LN, Young JB. Landsberg L. Differential catecholamine responses to dietary intake: effects of macronutrients on dopamine and epinephrine excretion in the rat. Metabolism 1989;38:91-9.
- Alexander RW, Gill JR Jr, Yamabe H, Lovenberg W, Keiser HR. Effects of dietary sodium and of acute saline infusion on the interrelationship between dopamine excretion and adrenergic activity in man. J Clin Invest 1974;54:194-200.
- Williams M, Young JB, Rosa RM, Gunn S, Epstein FH, Landsberg L. Effect of protein ingestion on urinary dopamine excretion: evidence for the functional importance of renal decarboxylation of circulating 3,4-dihydroxyphenylalanine in man. J Clin Invest 1986;78: 1687-93.
- Bell B, Rose CL, Damon A. The Normative Aging Study: an interdisciplinary and longitudinal study of health and aging. Aging Hum Dev 1972;3:5-17.
- Landsberg L, Troisi R, Parker D, Young JB, Weiss ST. Obesity, blood pressure and the sympathetic nervous system. Ann Epidemiol 1991;1:295-303.
- 13. Troisi RJ, Weiss ST, Parker DR, Sparrow D, Young JB, Landsberg L. Relation of obesity and diet to sympathetic nervous system activity. Hypertension 1991;17:669-77.
- Sampson L. Food frequency questionnaires as a research instrument. Clin Nutr 1985;4:171–8.
- Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122:51-65.
- Willett WC. Nutritional epidemiology. New York: Oxford University Press. 1990.
- Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh C-C. Physical activity. all-cause mortality, and longevity of college alumni. N Engl J Med 1986;314:605-13.
- Smedes F, Kraak JC, Poppe H. Simple and fast solvent extraction system for selective and quantitative isolation of adrenaline, noradrenaline and dopamine from plasma and urine. J Chromatogr 1982:231:25--39.
- Macdonald IA, Lake DM. An improved technique for extracting catecholamines from body fluids. J Neurosci Methods 1985;13:239-48
- SAS Institute Inc. SAS user's guide: statistics. 5th ed. Cary, NC: SAS Institute, 1985.
- Linnoila M, Oliver J, Adinoff B, Potter WZ. High correlations of norepinephrine, dopamine, and epinephrine and their major metabolite excretion rates. Arch Gen Psychiatry 1988;45:701-4.
- Reynolds V. Jenner DA, Palmer CD, Harrison GA. Catecholamine excretion rates in relation to life-styles in the male population of Otmoor, Oxfordshire. Ann Hum Biol 1981;8:197-209.
- Grantham JJ, Chonko AM. Renal handling of organic anions and cations; metabolism and excretion of uric acid. In: Brenner BM, Rector FC Jr, eds. The kidney. Vol 1. 3rd ed. Philadelphia: WB Saunders, 1986:663-700.
- Horky K, Marek J, Kopecká J, Gregorová I. Influence of age on orthostatic changes in plasma renin activity and urinary catecholamines in man. Physiol Bohemoslov 1975;24:481-8.
- Moyer TP, Jiang N-S, Tyce GM, Sheps SG. Analysis for urinary catecholamines by liquid chromatography with amperometric detection: methodology and clinical interpretation of results. Clin Chem 1979;25:256-63.
- Lehmann M, Spöri U, Keul J. [24-h-urinary excretion of free dopamine, noradrenaline and adrenaline in 190 male individuals

- related to age and blood pressure]. Klin Wochenschr 1985;63: 268-71.
- Jenner DA, Harrison GA, Prior IAM, Leonetti DL, Fujimoto WY.
   24-h catecholamine excretion: relationships with age and weight. Clin Chim Acta 1987;164:17-25.
- Kärki NT. The urinary excretion of noradrenaline and adrenaline in different age groups, its diurnal variation and the effect of muscular work on it. Acta Physiol Scand [Suppl] 1956;39:1-96.
- Muskiet FAJ, Thomasson CG, Gerding AM, Fremouw-Ottevangers DC, Nagel GT, Wolthers BG. Determination of catecholamines and their 3-O-methylated metabolites in urine by mass fragmentography with use of deuterated internal standards. Clin Chem 1979;25:453– 60.
- Fogari R, Marchesi E, Altieri S. Urinary dopamine in the aged. Boll Soc Ital Biol Sper 1977;53:133-6.
- Clark BA, Young JB, West C, Elahi D, Epstein FH. Decline in urinary excretion of dopamine and PGE2 with age. Clin Res 1991;39: 226A(abstr).

- Fukagawa NK, Bandini LG, Rowe JW, Young JB. Effect of age on renal responses to protein ingestion in man. Clin Res 1989;37: 490A(abstr).
- Leonetti DL, Bergstrom RW, Shuman WP, et al. Urinary catecholamines, plasma insulin and environmental factors in relation to body fat distribution. Int J Obes 1991;15:345-57.
- Schwartz RS, Jaeger LF, Veith RC. The importance of body composition to the increase in plasma norepinephrine appearance rate in elderly men. J Gerontol 1987;42:540-51.
- Rocchini AP, Katch V, Kveselis D, et al. Insulin and renal sodium retention in obese adolescents. Hypertension 1989;14:367-74.
- Yale JF, Leiter LA, Marliss EB. Metabolic responses to intense exercise in lean and obese subjects. J Clin Endocrinol Metab 1989;68: 438-45.
- Gustafson AB, Farrell PA, Kalkhoff RK. Impaired plasma catecholamine response to submaximal treadmill exercise in obese women. Metabolism 1990;39:410-7.